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7-乙酰基-鲁山冬凌草甲素,紫萼香茶菜甲素及其有关二萜化合物的结构修正

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摘要 从无毛狭叶香茶菜(*Isodon angustifolius* var. *glabrescens* H. W. Li)中分离得到4个已知二萜化合物: 7-乙酰基-鲁山冬凌草甲素,鲁山冬凌草甲素、乙素和紫萼香茶菜甲素,经二维核磁共振波谱(2D-NMR)解析表明,它们的结构分别由先前报道的5, 6, 7和8应修订为结构1, 2, 3和4。

关键词 无毛狭叶香茶菜,7-乙酰基-鲁山冬凌草甲素,鲁山冬凌草甲素、乙素和紫萼香茶菜甲素结构修订

REVISION OF THE STRUCTURES OF 7-ACETYL-LUSHANRUBESCENSIN A, RABDOFORRESTIN A, AND RELATED DITERPENOIDS

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Abstract Four known diterpenoids 7-acetyl-lushanrubescensin A, Lushanrubescensin A and B, and rabdoforrestin A have also been isolated from *Isodon angustifolius* var. *glabrescens*, and their structures have revised to 1, 2, 3, and 4 from the structures 5, 6, 7 and 8 reported previously by the spectral analysis, especially on the basis of 2D NMR data in this paper.

Key words *Isodon angustifolius* var. *glabrescens*, 7-acetyl-lushanrubescensin A, Lushanrubescensin A and B, Rabdoforrestin A, Revised structures

INTRODUCTION

Lushanrubescensin A and B have been isolated from *Rabdosia rubescens* as the major constituents and reported to have the structure (6) (Qing *et al*, 1984) and (7) (Li *et al*, 1986) on the basis of interpretation of the spectroscopic data and the results of chemical reactions. 7-acetyl-lushanrubescensin A (5) has also been prepared from 6 as derivative, and reported to have the structure (5) in previous paper. On the other hand, rabdoforrestin A has been isolated from *Rabdosia forrestii*, and reported to have the structure (8)

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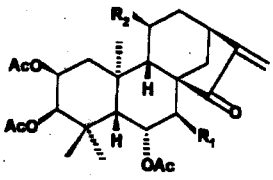
(Sun *et al*, 1988) by comparisons of its spectral data with lushanrubescensin B and chemical correlation with 7-acetyl-lushanrubescensin A. During the course of our studies on the chemical constituents of *Isodon angustifolius* var. *glabrescens*, 7-acetyl-lushanrubescensin A, lushanrubescensin A and B and rabdoforrestin A have also been isolated from this plant. We reexamined those structures reported previously and reached the conclusion that their structures should be revised, because the configurations of the substituents of 7-acetyl-lushanrubescensin A, lushanrubescensin A at C-7 and C-11 position, and those of lushanrubescensin B and rabdoforrestin A at C-11 were found to be assigned incorrectly in previous paper. This paper deal with the isolation of 7-acetyl-lushanrubescensin A, lushanrubescensin A, B and rabdoforrestin A from *Isodon angustifolius* var. *glabrescens* and revision of their structures.

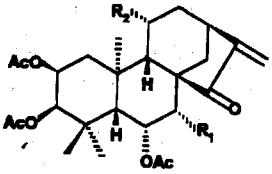
RESULTS AND DISCUSSION

7-acetyl-lushanrubescensin A(1), $C_{30}H_{40}O_{11}$([M+1]$^+$m / z 577), mp 185～ 186℃ , was obtained as colorless crystals from MeOH. It was verified to be same compound as that reported previously by co-TLC, IR and ^{1}H NMR with authentic sample. We re-examined the structure (*ent*-2α, 3α, 6β, 7β, 11β--pentaacetoxy-kaur-16-ene-15-one) reported previously and reached the conclusion that the structure of 7-acetyl-lushanrubescensin A should be revised, because the configuration of the acetoxyl groups at C-11 and C-7 were found to be assigned incorrectly in previous paper. 7-acetyl-lushanrubescensin A had the ent-kaur-16-en-15-one structure as the basic skeleton from the reported spectral data. In addition to the basic skeleton, it contained five acetoxyl group judged from NMR data [δ2.24(s), 2.13(s), 2.09(s), 1.96(s), 1.75(s) for acetyl in ^{1}H NMR, and δ170.47(s), 170.33(s), 169.56(s), 169.38(s), 169.09(s) for ester carbonyl in ^{13}C NMR]. The location of five acetoxyl groups were examined by ^{1}H-^{1}H COSY , which further confirmed by ^{1}H-^{13}C COSY experimental. In the ^{1}H-^{1}H COSY spectrum of 1, following connections were observed. The connectivities for H-3α(δ5.30, d, J = 2.8Hz)→H-2α(δ5.48, ddd, J = 12.5, 4.1, 2.8Hz)→H-1α(δ2.24, m)→H-1β(δ2.09, m) indicated two acetoxyl groups should be located at C-3 and C-2 position, respectively. The stereochemistry was deduced to be 3β-OAc and 2β-OAc from the coupling patterns of H-3 and H-2. The connection for H-7α(δ5.54, d, J = 3.5Hz)→ H-6β(δ5.36, dd, J = 3.5, 1.4Hz)→H-5β(δ2.38, brs) showed two acetoxyl groups should be attach to C-7 and C-6 position, respectively. The configuration should be 7β-OAc and 6α-OAc judged from coupling patterns of H-7 , H-6 and H-5. The chemical shift of C-5(δ43.37) showed a special upfield shift owing to the strong γ-gauche effect of the C-3β and C-7β disubstituents, which further indicated that the two acetoxyl group at C-3 and C-7 position must be in the β-orientation(Gouzallz *et al*, 1981). The configuration of H-7 assigned incorrectly in previous paper was ascribed to adopted a noise C-5 signal. The connections for H-11α(δ5.38, brd, J = 4.4Hz) → H-12α(δ2.20, m)→ H-12β(δ2.01, m)→ H-13β(δ2.95, brs)→ H-14β(δ1.47, dd, J = 12.4, 3.7Hz) → H-14α(δ2.64, d, J = 12.4Hz) indicated that an acetoxyl group must be located at C-11 position. The stereochemistry was deduced to be 11β-OAc from the coupling constants of H-11α. The signal of H-11α was coupled with H-12α, whereas the signal showed only small coupling with H-12β and H-9βsince the dihedral angles of H-11α with H-12β and H-9β are near 90 ° respectively, similar to the case of inflexin(Takeda *et al*, 1988). This conclusion was also confirmed by the fact that the signal of H-11α(δ5.48) had no correlation peaks with H-9β(δ2.37) and H-12β(δ2.01) in ^{1}H-^{1}H COSY spectrum of 1. The configuration of H-11 was assigned incorrectly in previous paper owing to no detailed analysis of ^{1}H NMR data.

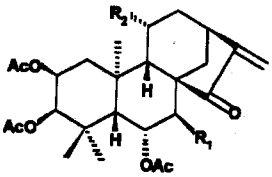
Therefore, 7-acetyl-lushanrubescensin A was revised to 1 from 5.



1. R_1=OAc, R_2=OAc
2. R_1=OH, R_2=OAc
3. R_1=OH, R_2=OH
4. R_1=OAc, R_2=OH



5. R_1=OAc, R_2=OAc
6. R_1=OH, R_2=OAc



7. R_1=OH, R_2=OH
8. R_1=OAc, R_2=OH

Lushanrubescensin A(2), $C_{28}H_{38}O_{10}[M+1]^+$ m/z 535, was obtained as colorless crystals from MeOH. It was verified to be same compound as that reported previously by co-TLC, IR and ^{1}H NMR with original sample isolated from Rabdosia rubescens. This compound has been elucidated to have the structure **6** by chemical correlation with **5** in previous paper(Li *et al*, 1986). Based on the revised structure **5**, the structure of lushanrubescensin A should be also revised to **2** from **6**.

Table 1 ^{13}C NMR data of compounds **1**~**4** (pyridine-d_5)

C	1	2	3	4	C	1	2	3	4
1	40.93 t	40.79 t	40.82 t	40.89 t	16	150.18 s	150.16 s	150.95 s	151.08 s
2	67.52 d	67.63 d	67.85 d	67.33 d	17	113.25 t	114.56 t	112.86 t	111.44 t
3	77.55 d	77.64 d	77.78 d	77.70 d	18	28.01 q	27.99 q	28.01 q	27.97 q
4	38.30 s	38.29 s	38.28 s	37.41 s	19	22.97 q	23.24q	23.26 q	22.91q
5	43.37 d	41.98 d	42.11 d	43.33 d	20	20.44 q	20.63 q	20.65 q	20.53 q
6	69.72 d	71.20 d	71.47 d	70.07 d	O	170.47 s	170.60 s	170.55 s	170.31 s
7	71.22 d	73.13 d	73.71 d	71.55 d	Ac	170.33 s	170.35 s	170.30 s	170.31 s
8	48.48 s	50.02 s	49.89 s	48.46s		169.56 s	169.75 s	169.86 s	169.61 s
9	55.44 d	55.00 d	59.14 d	59.12 d		169.38 s	169.02 s	21.34q	169.42 s
10	39.74 s	39.78 s	39.40 s	38.28 s		169.09 s	21.22 q	21.33 q	21.73 q
11	68.09 d	68.29 d	64.97 d	64.90 d		21.24 q	20.92 q	21.01 q	21.32 q
12	38.12 t	38.29 t	40.82 t	40.89 t		21.15 q	20.63 q		21.17 q
13	36.70d	37.37 d	38.13d	36.52d		21.15 q	20.63 q		20.53 q
14	35.06 t	34.50 t	35.22 t	35.53 t		20.92 q			
15	204.41 s	212.71 s	213.63 s	204.69 s		20.55 q			

Lushanrubescensin B(3), $C_{26}H_{36}O_9$([M]$^+$ m/z 492) was obtained colourless crystals from MeOH. It was verified to be same compound as that reported previously by co-TLC, IR and ^{1}H NMR with authentic sample isolated from Rabdosia rubescens. This compound has been elucidated to have the structure **7** by chemical correlation with **5** in previous paper (Sun *et al*, 1988). Based on the revised structure **5**, the structure of lushanrubescensin B should be also revised to **3** from **7**.

Rabdoforrestin A(4), $C_{28}H_{38}O_{10}$([M]$^+$ m/z 534), was obtained as colorless crystals from MeOH. It was verified to be same compound as that reported previously by co-TLC, IR and ^{1}H NMR with authentic sample isolated from Rabdosia forrestii. This compound has been elucidated to have the structure **8** compared with lushanrubescensin A(6) in reference (Gouzallz *et al*, 1981). Based on the revised structure **5**, the structure of rabdoforrestin A should be also revised to **4** from **8**.

EXPERIMENTAL

General. mps: uncorr. UV: MeOH; IR: KBr; EIMS: 70eV; ^{1}H and ^{13}C NMR: 400Hz and 100Hz, with TMS int. stard. Chemical shift value were reported in δ(ppm) units using pyridine-d_5 as solvent.

Plant material: plant material was collected in Dali county, Yunnan province, China, in Sept., 1993, and identified as *I. angustifolius* (Dunn) var. *glabrescens.* by Prof. Li Xi-Wen. A voucher specimen is deposited in the herbarium of the Department of Taxonomy, Kunming Institute of Botany, the Chinese Academy of Sciences.

Extraction and isolation. The dried leaves (3.00kg) were extract with EtOH (5L × 3) under reflux temperatures. The extract was concentrated in vacuum to give residue (300g) which was chromatographed over silica gel(200～300 mesh, 1.5kg). The column was eluted with $CHCl_3$-Me_2CO(9.5: 0.5, 9:1, 8:2, 7:3, 6:4) and Me_2CO as solvent to afford 12 fraction. The fr.3 were further purified by cc[si gel, pet. ether: Me_2O(8: 2)], and gave **1**(800 mg), **2**(227 mg), **4**(280 mg). The fr. 4 were further purified by cc si gel, $CHCl_3$: Me_2O(8: 2), and gave **3**(100 mg).

7-Acetyl-lushanrubescensin A (1), $C_{30}H_{40}O_{11}$, colorless crystals (MeOH), mp: 185～186℃, $[\alpha]_D^{22}$: -54.5° ($CHCl_3$, c 0.46), UV(MeOH) λ_{max}(logε) nm: 238(5.53); IRν_{max}^{KBr}cm^{-1}: 2920, 1735, 1645, 1370, 1245, 1030; ^{1}H NMR δ2.24(1H, overlap, H-1α), 2.09(1H, overlap, H-1β), 5.48(1H, ddd, J = 12.5, 4.1, 2.8Hz, H-2α), 5.30(1H, d, J = 2.8Hz, H-3α), 2.38(1H, brs, H-5β), 5.36(1H, dd, J = 3.5, 1.4Hz, H-6β), 5.54(1H, d, J = 3.5Hz, H-7α), 2.37(1H, brs, H-9β), 5.38(1H, brd, J = 4,4Hz, H-11α), 2.20(1H, m, H-12α), 2.01(1H, m, H-12β), 2.95(1H, brs, H-13α), 2.64(1H, d, J = 12.4Hz, H-14α), 1.47(1H, dd, J = 12.4, 3.7Hz, H-14β), 5.95(1H, brs, H-17a), 5,23(1H, brs, H-17b), 1.00(3H, s, Me-18), 1.26(3H,s Me-19), 1.58(3H, s, Me-20), 2.24, 2.13, 2.09, 1.96, 1,75(each 3H, s, 5 × Ac); EIMS m / z(rel. int.): 577[M+1]$^+$(2), 516[M-AcOH]$^+$(15), 474 [M-AcOH-COCH2]+(25), 456 [M-2 × AcOH]$^+$(15), 414 [M-2 × AcOH-$COCH_2$]$^+$(50), 396 [M-3 × AcOH]$^+$(32), 354 [M-3 × AcOH-$COCH_2$]+(40), 294 [M-4 × AcOH-$COCH_2$]$^+$(100), 279 [M-4 × AcOH-$COCH_2$-Me]$^+$(90); ^{13}C NMR see table 1.

Lushanrubescensin A (2), $C_{28}H_{38}O_{10}$, colorless crystals(MeOH), mp: 185～186℃, $[\alpha]_D^{22}$-49.07° (MeOH, c 0.54), UV(MeOH) λ_{max}(logε)nm: 240(5.96); IRν_{max}^{KBr}cm^{-1}: 3400, 2920, 1730, 1645, 1435, 1370, 1240, 1030; ^{1}H NMR δ 6.33(1H, brs, OH, D_2O exchange, disappear), 5.56(1H, ddd, J = 12.5, 4.0, 2.6Hz, H-2α), 5.30(1H, d, J = 2.6Hz, H-3α), 2.64(1H, brs, H-5β), 5,54(1H, dd, J = 3.4, 1.7Hz, H-6β), 4.02(1H, d, J = 3.4, H-7α), 2.40(1H, brs, H-9β), 5.36(1H, d, J = 4.3Hz, H-11α), 3.00(1H, brs, H-13α), 2.55(1H, d, J = 12.5Hz, H-14α), 1.48(1H, dd, J = 12.5, 3.6Hz, H-14β), 6.05(1H, brs, H-17a), 5.35(1H, brs, H-17b), 1.04(3H, s, Me-18), 1.12(3H, s Me-19), 1.49(3H, s, Me-20), 2.16, 2.05, 2.00, 1.91(each 3H, s, 4 × Ac); EIMS m / z(rel. int.): 535[M+1]$^+$(2), 474[M-AcOH]$^+$(8), 414 [M-2 × AcOH]$^+$(40), 354[M-3 × AcOH]$^+$(20), 312[M-3 × AcOH-$COCH_2$]$^+$(25), 294[M-4 × AcOH]$^+$(30), 279[M-4 × AcOH-Me]$^+$(80); ^{13}C NMR see table 1.

Lushanrubescensin B (3), $C_{26}H_{36}O_9$, colorless crystals(MeOH), mp: 182～184℃, $[\alpha]_D^{22}$: -78.5° (MeOH, c 0.52); UV(MeOH) λ_{max}(logε)nm: 240(5.81); IRν_{max}^{KBr}cm^{-1}: 3410, 2910, 1730, 1635, 1370, 1230, 1030; ^{1}H NMR δ : 5.54(1H, ddd, J = 12.0, 4.2, 2.8Hz, H-2α), 5.20(1H, d, J = 2.8Hz, H-3α), 2.58(1H, brs, H-5β), 5.45(1H, dd, J = 3.2, 1.4Hz, H-6β), 4.00(1H, d, J = 3.2Hz, H-7α), 2.55(1H, brs, H-9β), 4.34(1H, brs, H-11α), 3.03(1H, brs, H-13α), 2.58(1H, d, J = 12.6Hz, H-14α), 1.46(dd, J = 12.6, 3.4Hz, H-14β), 6.02(1H, brs, H-17a), 5.36(1H, brs, H-17b), 1.00(3H, s, Me-18), 1.13(3H, s, Me-19), 1.51(3H, s, Me-20), 2.13,

1.97, 1.95(each 3H, 3× Ac); EIMS m/z(rel. int.): 492[M]$^+$(2), 432[M−AcOH]$^+$(25), 414[M−AcOH−H_2O]$^+$(5), 372[M−2× AcOH]+(10), 312 [M−3× AcOH]+(100), 297[M−3× AcOH−Me]+(70); ^{13}C NMR see table 1.

Rabdoforrestin A (4), $C_{28}H_{38}O_{10}$, colorless crystals(MeOH), mp: 173～174℃, $[\alpha]_D^{22}$: −38.70° (MeOH, c 0.58), UV(MeOH) λ_{max}(logε)nm: 239.5(5.84); IRν_{max}^{KBr}cm^{-1}: 3480, 2910, 1735, 1649, 1415, 1220, 1030; ^{1}H NMR δ: 5.51(1H, ddd, J=12.3, 4.1, 2.4Hz, H−2α), 5.25(1H, d, J=2.4, H−3α), 2.58(1H, brs, H−5β), 5.35(1H, dd, J= 3.5, 1.5Hz, H−6β), 5.54(1H, d, J=3.5Hz, H−7α), 2.34(1H, brs, H−9β), 4.38(1H, brs, H−11α), 3.00(1H, brs, H−13α), 2.65(1H, d, J=12.2Hz, H−14α), 1.42(1H, dd, J=12.2, 3.5Hz, 14β−H), 5.90(1H, brs, H−17a), 5.20(1H, brs, 17b), 0.91(3H, s, Me−18), 1.11(3H, s, Me−19), 1.51(3H, s, Me−20), 2.28, 2.09, 2.02, 2.00(each 3H, s, 4× Ac); EIMS m/z(rel. int.): 534[M]$^+$(2), 474[M−AcOH]$^+$(5), 432 [M−AcOH−$COCH_2$]$^+$(100), 414 [M−2× AcOH]$^+$(40), 312[M−3× AcOH−$COCH_2$]$^+$(65), 294[M−3× AcOH−$COCH_2$−H_2O]$^+$(95), 279[M−4×AcOH−$COCH_2$−Me]$^+$(70); ^{13}C NMR see table 1.

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